

PATENT APPLICATION

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicants : Wenfeng Xu, Wayne Kindsvogel, Yasmin A. Chandrasekher,
Stacey R. Dillon, Joyce M. Lehner, Anthony W. Siadak, Pallavur
V. Sivakumar, Margaret D. Moore
Serial No. : 10/807,837
Filed : March 24, 2004
For : ANTI-IL-22RA ANTIBODIES AND BINDING PARTNERS
AND METHODS OF USING IN INFLAMMATION
Confirmation No. : 4419

Examiner : Stoica, E. G.
Art Unit : 1647
Docket No. : 03-02
Date : October 9, 2007

DO NOT ENTER
EGS 10/26/2007

Mail Stop AF
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 CFR §1.132

Sir:

I, WenFeng Xu, declare and say as follows:

1. I am a Principal Scientist in the Molecular and Cell-Based Discovery department at ZymoGenetics, Inc.

2. I am a named inventor in the above referenced Application, and I have read and understand the Specification and Claims of the above referenced Application. For example, I am familiar with the protocol and results of Example 28 of the above referenced Application.

3. I have read and understand the Office Action mailed May 7, 2007 (the "Present Office Action"). For Example, I understand that the Examiner has alleged the following: the prior art references (US Patent Application No. 02-0164689 (Busfield); Hopp et al. (PNAS 78: 3824-3828, 1981); and Lok et al. (US Patent No. 5,965,704) teach

an antibody that specifically binds to IL-22RA and *inherently* teach an antibody that reduces IL-22RA activity (e.g., IL-20 or IL-22 activity).

4. I disagree with the allegation that an antibody that specifically binds to IL-22RA necessarily reduces IL-22RA activity. **It is well understood in the art that an antibody that specifically binds to an antigen does not necessarily also neutralize or reduce the activity of the antigen.** This is because an antigen commonly has multiple epitopic regions where an antibody may bind; and if an antibody binds to an epitope that is outside or unrelated to a specific ligand-receptor binding domain, the antibody will specifically bind to the antigen, but it will not neutralize or reduce the activity associated with the specific ligand-receptor binding.


5. Example 28 of the above referenced Application describes a cell based neutralization assay. The factor-dependent pre-B cell line BaF3 co-transfected with IL-22RA and IL-20RB (pDIRS1) (BAF/IL-22RA/IL-20RB cells) was used to assess neutralization potential of anti-IL-22RA antibodies by antagonizing IL-20 on the IL-22RA/IL-20RB receptor. Similarly, BaF3 co-transfected with IL-22RA and IL-10RB (CRF2-4) (BAF/IL-22RA/CRF2-4 cells) was used to assess the neutralization potential of anti-IL-22RA antibodies by antagonizing IL-22 on the IL-22RA/IL10RB receptor. Proliferation in the presence of IL-20 or IL22 on its respective receptor-expressing cell line, and inhibition of such proliferation in the presence of the antagonist antibodies, was assessed using an Alamar blue assay. Inhibition of proliferation on these cells is indicative of neutralizing activity in this assay. This assay was performed to identify which IL-22RA antibodies specifically bind to IL-22RA and neutralize IL-22RA activity.

6. I attach herewith a table showing a sampling of the assay results from Example 28. Each line of the table represents a monoclonal antibody clone. 11D6, 2G5, and 2E4 are negative controls, they represent antibodies that do not specifically bind to IL-22RA and that do not reduce the IL-22RA activity of up-regulating cell proliferation via binding to IL-22.

Not all antibodies that specifically bind to IL-22RA necessarily neutralize IL-22RA activity. For example, note that several antibodies that specifically bind to IL-22RA do not reduce the IL-22RA the activity of up-regulating cell proliferation via binding to IL-22 (e.g. see clones 27, 84, and 85).

7. I further declare that statements made herein of my knowledge are true, and that all statements made on information are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Dated: 10-09-2007

By: 
ZymoGenetics, Inc.
WenFeng Xu, Ph.D.
Principal Scientist
Molecular and Cell-Based Discovery

Cell-based neutralization assay to test for anti-IL-22RA inhibition of IL-22

mAb clone	Binding to BaF3/IL22RA/IL10R B by FACS	Blocking IL22 activity in BaF3/IL22RA/IL10RB proliferaton assay
11	+	+
12	+	+
18	+	+
32	+	+
43	+	+
59	+	+
64	+	+
72	+	+
73	+	+
110	+	+
111	+	+
4	+	-
6	+	-
27	+	-
35	+	-
41	+	-
67	+	-
74	+	-
84	+	-
85	+	-
89	+	-
107	+	-
109	+	-
114	+	-
62	-	-
90	-	-
101	-	-
128	-	-
2E4	-	-
2G5	-	-
11D6	-	-

ATCC

#124
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**BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF
THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE**

INTERNATIONAL FORM

**RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3
AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.**

To: (Name and Address of Depositor or Attorney)

ZymoGenetics, Inc.
Attn: Elin Florkiewicz
1201 Eastlake Avenue East
Seattle, WA 98102

Deposited on Behalf of: ZymoGenetics, Nic.

Identification Reference by Depositor:

Patent Deposit Designation

SP2/0 mouse myeloma x rat spleenocyte hybridoma: R2.1.1G11.1
SP2/0 mouse myeloma x rat spleenocyte hybridoma: R2.1.12G7.1
SP2/0 mouse myeloma x rat spleenocyte hybridoma: R2.1.13C8.1

PTA-6035
PTA-6036
PTA-6037

The deposits were accompanied by: a scientific description a proposed taxonomic description indicated above. The deposits were received June 3, 2004 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested June 9, 2004. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris
Marie Harris, Patent Specialist, ATCC Patent Depository

Date: June 28, 2004

cc: Jennifer K. Johnson

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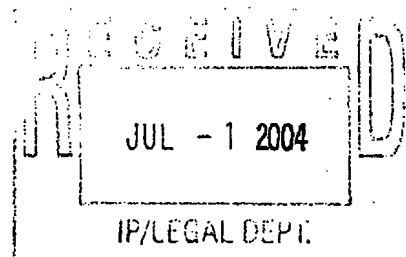
BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.

To: (Name and Address of Depositor or Attorney)

ZymoGenetics, Inc.
Attn: Ursula Garrigues
1201 Eastlake Avenue East
Seattle, WA 98102



Deposited on Behalf of: ZymoGenetics, Nic.

Identification Reference by Depositor:

Patent Deposit Designation

SP2/0 mouse myeloma x rat spleenocyte hybridoma: R2.1.5F4.1
SP2/0 mouse myeloma x rat spleenocyte hybridoma: R2.1.5H8.1

PTA-6024
PTA-6025

The deposits were accompanied by: a scientific description, a proposed taxonomic description indicated above. The deposits were received June 2, 2004 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

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The viability of the cultures cited above was tested June 9, 2004. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris
Marie Harris, Patent Specialist, ATCC Patent Depository

Date: June 28, 2004

cc: Jennifer K. Johnson

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BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

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To: (Name and Address of Depositor or Attorney)

ZymoGenetics, Inc.
Attn: Jeremy F. Capalungan
1201 Eastlake Avenue East
Seattle, WA 98102

Deposited on Behalf of: ZymoGenetics, Inc.

Identification Reference by Depositor:

Patent Deposit Designation

SP2/0 mouse myeloma x rat spleenocyte hybridoma: R2.1.15E2.1 Z13,157	PTA-6038
SP2/0 mouse myeloma x rat spleenocyte hybridoma: R2.1.16C11.1 Z13,155	PTA-6039
SP2/0 mouse myeloma x rat spleenocyte hybridoma: R2.1.18C8.1 Z13,156	PTA-6040

The deposits were accompanied by: a scientific description a proposed taxonomic description indicated above. The deposits were received June 3, 2004 by this International Depository Authority and have been accepted.

AT YOUR REQUEST: X We will inform you of requests for the strains for 30 years.

The strains will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strains, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strains.

If the cultures should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace them with living cultures of the same.

The strains will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the cultures cited above was tested June 9, 2004. On that date, the cultures were viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris
Marie Harris, Patent Specialist, ATCC Patent Depository

Date: June 28, 2004

cc: Jennifer K. Johnson

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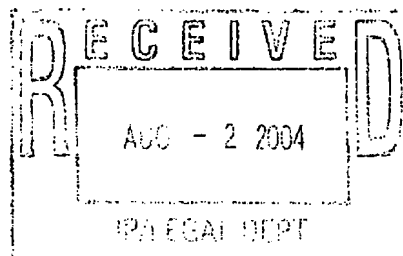
BUDAPEST TREATY ON THE INTERNATIONAL RECOGNITION OF THE DEPOSIT OF MICROORGANISMS FOR THE PURPOSES OF PATENT PROCEDURE

INTERNATIONAL FORM

RECEIPT IN THE CASE OF AN ORIGINAL DEPOSIT ISSUED PURSUANT TO RULE 7.3 AND VIABILITY STATEMENT ISSUED PURSUANT TO RULE 10.2

To: (Name and Address of Depositor or Attorney)

ZymoGenetics, Inc.
Attn: Ursula Garrigues
1201 Eastlake Avenue E
Seattle, WA 98102



Deposited on Behalf of: ZymoGenetics, Inc.

Identification Reference by Depositor:

Patent Deposit Designation

SP2/0 mouse myeloma x rat splenocyte hybridoma: R2.1.21G8.2

PT-6111

The deposit was accompanied by: ☐ a scientific description ☐ a proposed taxonomic description indicated above.

The deposit was received June 24, 2004 by this International Depository Authority and has been accepted.

AT YOUR REQUEST: ☒ We will inform you of requests for the strain for 30 years.

The strain will be made available if a patent office signatory to the Budapest Treaty certifies one's right to receive, or if a U.S. Patent is issued citing the strain, and ATCC is instructed by the United States Patent & Trademark Office or the depositor to release said strain.

If the culture should die or be destroyed during the effective term of the deposit, it shall be your responsibility to replace it with living culture of the same.

The strain will be maintained for a period of at least 30 years from date of deposit, or five years after the most recent request for a sample, whichever is longer. The United States and many other countries are signatory to the Budapest Treaty.

The viability of the culture cited above was tested June 29, 2004. On that date, the culture was viable.

International Depository Authority: American Type Culture Collection, Manassas, VA 20110-2209 USA.

Signature of person having authority to represent ATCC:

Marie Harris
Marie Harris, Patent Specialist, ATCC Patent Depository

Date: July 29, 2004

cc: Jennifer K. Johnson